(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 January 2001 (04.01.2001)

PCT

(10) International Publication Number
WO 01/00676 A1

(51) International Patent Classification[7]: C07K 14/655, 7/02, A61K 38/31, A61P 5/02, G01N 33/68

(21) International Application Number: PCT/US00/17401

(22) International Filing Date: 23 June 2000 (23.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/141,028 25 June 1999 (25.06.1999) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 60/141,028 (CIP)
Filed on 25 June 1999 (25.06.1999)

(71) Applicant *(for all designated States except US)*: **SOCIETE DE CONSEILS DE RECHERCHES ET D'APPLICATIONS SCIENTIFIQUES S.A.S.** [FR/FR]; 51, 53 rue du Docteur Blanche, F-75016 Paris (FR).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **MORGAN, Barry, A.** [US/US]; 237 Prospect Street, Franklin, MA 02038 (US). **SADAT-AALAEE, Dean** [US/US]; 37 Brookdale Circle, Shrewsbury, MA 01545 (US).

(74) Agent: **TSAO, Y., Rocky**; Fish & Richardson P.C., 225 Franklin Street, Boston, MA 02110-2804 (US).

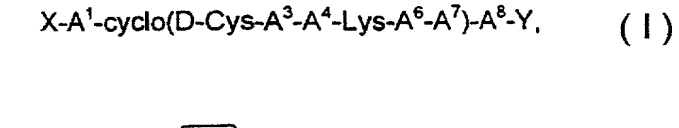
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

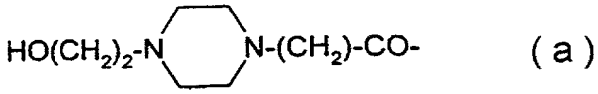
Published:
— *With international search report.*
— *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

[Continued on next page]

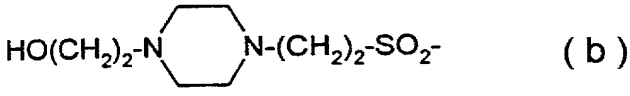
(54) Title: SOMATOSTATIN AGONISTS



(I)



(a)



(b)

(57) Abstract: The present invention is directed to cyclic peptides of formula (I): X-A^1-cyclo(D-Cys-A^3-A^4-Lys-A^6-A^7)-A^8-Y, or a pharmaceutically acceptable salt thereof, wherein X is H, formula (a) or formula (b); A^1 and A^3 are each independently the D- or L-isomer of an amino acid selected from the group consisting of Phe, Tyr, Tyr(I), Trp, 3-Pal, 4-Pal, Cpa and Nal; A^4 is L-Trp, D-Trp, L-β-methyl-Trp or D-β-methyl-Trp; A^6 is -NH-$(CHR^1)_n$-CO-, where n is 2, 3, or 4; A^7 is L- or D-Cys; A^8 is the D- or L-isomer of an amino acid selected from the group consisting of Phe, Tyr, Tyr(I), Trp, Nal, Cpa, Val Leu, Ile, Ser and Thr; Y is NR^2R^3 where R^2 and R^3 are each independently H or $(C_1$-$C_5)$alkyl; R^1 is selected from the group consisting H, $(C_1$-$C_4)$alkyl and -CH_2-aryl; wherein said aryl is an optionally substituted moiety selected from the group consisting of phenyl, 1-naphthyl, and 2-naphthyl, wherein said optionally substituted moiety is optionally substituted with one or more substituents each independently selected from the group consisting of (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, aryl, aryl(C_{1-6})alkyl, (C_{1-6})alkoxy, -$N(R^4R^5)$, -COOH, -$CON(R^4R^5)$, halo, -OH, -CN, and -NO_2; R^4 and R^5 each is, independently for each occurrence, H or (C_{1-3})alkyl; where the Cys of A^2 is bonded to the Cys of A^7 by a di-sulfide bond formed from the thiol groups of each Cys; pharmaceutical compositions comprising said peptides and the use thereof as a somatostatin receptor subtypes agonist. The peptides of the present invention bind selectively to the somatostatin subtype receptor type-5 and elicit an agonist effect from the somatostatin subtype receptors that the peptides bind to.

WO 01/00676 A1